REMARKS / ARGUMENTS

I. Amendments to the specification, drawings and claims

Figure 3, as well as the descriptions of Figures 3 and 4 at page 10, refer incorrectly to "pCAmg002". These are typographical errors. Figure 4 refers correctly to pCAmgp002. Figure 3 and page 10 have been amended to correct the error.

Claims 8-11, 35, 36 and 38 remain in this application. Claims 42-45 have been added.

Claims 8-11 and 38 have been amended to more clearly and particularly claim the invention.

Claim 8 has been amended to be drawn to --A vaccine vector-- rather than to "A vaccine comprising a vaccine vector", and to delete reference to the nucleic acid molecule being "integrated and expressed in a bacterial cell suitable for use as a vaccine vector".

Claims 8, 10 and 38 have been amended to delete parts (b) and (c), and to replace "one or more control sequences" with --a promoter--, as supported at page 29, lines 7-30.

Claim 9 has been amended to further clarify that --the additional polypeptide is a *Chlamydia* polypeptide--.

Claim 11 has been amended to further clarify that the claim is drawn to --A vaccine comprising the vaccine vector of claim 8 and a pharmaceutically acceptable carrier--.

Claim 38 has been amended to correct antecedent basis for "The vaccine vector of claim 8".

Because these amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

Dependent claims 42-45 have been added which are drawn to the vaccine vector of claim 8, the composition of claim 10, the vaccine of claim 11, and the vaccine vector of claim 38, respectively, wherein the promoter is specified as the CMV promoter. Support for the new claims is found at least at page 29, lines 20-21, as well as page 49, lines 6-10 and Examples 2 and 3 at pages 49-51. The Examiner is respectfully requested to enter and examine claims 42-45.

Applicants retain the right to present claims drawn to the cancelled subject matter in a divisional application(s).

II. Election/Restriction

The Examiner has stated that new claims 38, 40 and 41 have been withdrawn from consideration because they are drawn to "non-elected invention". The Examiner has further stated that only species SEQ ID NO: 1 or nucleic acids encoding SEQ ID NO: 2 are examined, and that claims 3-6, 9, 35-38, 40, 41 as well as a number of subparagraphs of claims 8, 10, 11 and 39 drawn to non-elected species "stand withdrawn from consideration". The Examiner has further stated that claims 8, 10, 11 and 39 "recite non-elected inventions" and that "appropriate correction is required." Applicants traverse on the grounds that the Examiner's election/restriction practice is improper.

In a previously-filed response to the Restriction requirement, claims 1-14, 19, 35 and 36 (Group I) was elected, with Species 1 being provisionally elected. In the response filed April 21, 2003, Applicants pointed out that generic claims need not be limited to the elected species, and claims not directed to the elected species need not be cancelled in response to the species election requirement, in accordance with MPEP 806.04(d) and MPEP 806.04(f).

With respect to claims 38, 40 and 41, Section 821.03 of the MPEP refers to restriction of new claims drawn to an invention distinct from, or independent of, the invention previously claimed. Since claims 38, 40 and 41 are drawn to the subject matter of old claim 8, which is part of restriction Group I, these claims should properly be examined as part of Group I.

With respect to the Examiner's (repeated) requirement that "appropriate correction" be made to remove "non-elected inventions", this requirement is improper. The claims had been earlier amended to remove non-elected subject matter, i.e. subject matter of Groups II to IX. Species are by definition not independent and distinct inventions (MPEP 806.04(a)). If claims are to be restricted to different species, they must be mutually exclusive (MPEP 806.04 (f)). Thus the subject matter of non-elected species should not be cancelled because species election is not a restriction requirement. The election of species is a provisional election. In Applicants' understanding, once the claims to the elected species is found to be allowable, the Examiner would move on to examine the next species.

Applicants point out there are undesirable consequences if the non-elected species were to be cancelled and refiled in a divisional application. First, there would be significant fees for filing separately for the species. Secondly, a terminal disclaimer may be required for the subsequent divisional applications.

To advance prosecution, claims 8, 10 and 38 have been amended to remove parts (b) and (c) and claims 39-41 have been cancelled. The Examiner is respectfully requested to examine all the pending claims as well as new claims 42-45 which depend on claims 8, 10, 11 and 38, respectively.

III. Rejection of Claims 8, 10, 11 and 39 Under 35 U.S.C. § 112, First Paragraph

The Examiner has maintained that claims 8, 10, 11 and 39 lack enablement for utilization of SEQ ID NO:1 and nucleic acid sequences encoding SEQ ID NO:2 as a vaccine or pharmaceutical composition. Applicants respectfully traverse.

Applicants have pointed out in the earlier response that immunization *in vivo* using a DNA construct expressing SEQ ID NO:2, i.e. pCAmgp002 (Figure 3), resulted in immune protection (Table 1 and Figure 4). The Examiner's position in response to this is that "the embodiment used to traverse the scope of enablement rejection is not claimed. Figure 4 also shows an outer membrane protein of Chlamydia that did not produce a protective immune response (pCABk917). Induction of a protective immune response is unpredictable in the art and this fact is supported by the data provided in Figure 4."

The Examiner's position is not understood. pCABk917 is the control construct which expresses a polypeptide unrelated to SEQ ID NO:2 (see page 51, lines 7-20). That is why pCABk917 did not induce a protective immune response. Attached to this response is a Declaration from inventor Andrew Murdin, showing that the protein sequences of the (protective) pCAmgp002 and the (control) pCABk917 are unrelated.

The Examiner has stated that claim 8 recites "one or more control sequences for expression of the polypeptide in a mammalian cell", which the Examiner alleged to include the sequence ATG. Applicants traverse. A skilled person would not consider ATG to be an expression control sequence. Nevertheless, to advance prosecution, claim 8 (and 10) have been amended to replace this phrase with "a promoter".

The Examiner has stated that "The instantly claimed invention does not comprise the critical pCMV virus promoter". Applicants submit that pCMV is not "critical". Rather, numerous promoters are suitable, as stated at page 29, lines 12-30 of the specification:

> Use of the polynucleotides of the invention include their administration to a mammal as a vaccine, for therapeutic or prophylactic purposes. Such polynucleotides are used in the form of DNA as part of a plasmid that is unable to replicate in a mammalian cell and unable to integrate into the mammalian genome. Typically, such a DNA molecule is placed under the control of a promoter suitable for expression in a mammalian cell.

> The promoter functions either ubiquitously or tissue-specifically. Examples of non-tissue specific promoters include the early Cytomegalovirus (CMV) promoter (described in U.S. Patent No. 4,168,062) and the Rous Sarcoma Virus promoter (described in Norton & Coffin, Molec. Cell Biol. (1985) 5:281). An example of a tissue-specific promoter is the desmin promoter which drives expression in muscle cells (Li *et al.*, Gene (1989) 78:243, Li & Paulin, J. Biol. Chem. (1991) 266:6562 and Li & Paulin, J. Biol. Chem. (1993) 268:10403). Use of promoters is well-known to those skilled in the art. Useful vectors are described in numerous publications, specifically WO 94/21797 and Hartikka *et al.*, Human Gene Therapy (1996) 7:1205.

Applicants further submit a second Declaration from inventor Murdin showing the results of different vaccine vectors containing different promoters expressing a known protective protein from Chlamydia, in the same mouse animal model as described in Example 3 of the specification. Dr. Murdin's Declaration clearly demonstrates that as long as the protective antigen is expressed in the host by an effective promoter, the protective results are consistent and reproducible. Thus Applicants submit that the scope of the claims enabled and the claims need not be restricted to pCMV promoter.

The Examiner has noted that Figure 3 shows "pCAmg002" whereas Figure 4 shows "pCAmgp002". Reference to pCAmg002 is a typographical error. Figure 3, as well as the descriptions of Figures 3 and 4 at page 10, have been corrected to refer to pCAmgp002.

The Examiner has stated that "No compositions that comprise any bacterial cell that comprises SEQ ID NO 2 have been shown to induce a protective immune response." The claims have been amended to delete the phrase "wherein the nucleic acid molecule... is integrated and expressed in a bacterial cell suitable for use as a vaccine vector."

In view of the above, Applicants submit that the scope of the claims, as amended, comply with 35 U.S.C. § 112, first paragraph. Withdrawal of the rejection is respectfully requested.

IV. Rejection of the Claims Under 35 U.S.C. § 102(a)

The Examiner has maintained the rejection of claims 8, 10, 11 and 39 under 35 U.S.C 102(a) as being anticipated by Kalman et al. Applicants traverse this ground for rejection.

The Examiner states that *C. pneumoniae* CWL029 disclosed by Kalman et al. comprises SEQ ID NO:1 integrated into the bacterial chromosome and expressed the encoded outer membrane protein SEQ ID NO:2. The Examiner alleged that claim 8 reads on CWL029 because the claim does not require that the nucleic acid be heterologous to the host bacteria, and because ATG is allegedly an expression control sequence.

Claim 8 has been amended to delete the phrase "wherein the nucleic acid molecule... is integrated and expressed in a bacterial cell suitable for use as a vaccine vector." Claims 8 and 10 have been amended to replace "one or more control sequences for expression of the polypeptide in a mammalian cell" with "a promoter". As amended, the claims do not read on CWL029.

The Examiner states that Kalman et al. determined the encoded protein's functionality to be polymorphic outer membrane protein, Family G, and that Kalman provided "expression data by disclosing data on a new family of chlamydial polymorphic membrane proteins, encoded and expressed in bacterial strain CWL029".

The Examiner's contention that Kalman discloses the function as polymorphic outer membrane protein, Family G, at page 388, col. 1, is not understood. There is no reference here to outer membrane protein, Family G, or to Cpn0021. In fact, SEQ ID NO 2 is <u>not</u> a Family G polymorphic outer membrane protein; (evidence of this can be submitted if required by Examiner).

Genbank Accession AE001587 AE001363 does indicate that CPn0021 (at position 11484... 13190) is a "Predicted OMP [leader peptide]", but this does not

mean that the sequence was expressed. In fact, there is no evidence whatsoever that Kalman et al. has expressed SEQ ID NO:1. The functionalities assigned to the sequences by Kalman et al. are inferred based on similarity searching of the sequence database. As stated at page 386, left column of Kalman et al.:

> We analysed the 1,230,230-nt (%G+C 40.6) *C. pneumoniae* genome and identified 1,073 likely protein-coding genes. Similarity searching permitted the inferred functional assignment of 636 (60%) genes, and 251 (23%) are similar to hypothetical genes for other bacterial organisms, including *C. trachomatis*. The remaining 186 (17%) are not homologous to sequences deposited in Genbank.

As stated in our earlier response, Kalman et al. has sequenced the entire genome of two Chlamydia strains by cloning random fragments into a M13 vector for automated sequencing. No expression data is shown. Kalman et al. does not disclose or suggest expressing the sequences. Kalman's sequences lack the structural feature of being operatively linked to a promoter for expression of the polypeptide in a mammalian cell, as specified in the claims.

Since Kalman's sequences are not in expressible form and are not capable of performing the intended use, Kalman et al. does not anticipate the vaccines and compositions of the present application.

Withdrawal of the rejection under 35 U.S.C. §102(a) in view of Kalman et al., is respectfully requested.

V. Concluding Remarks

In view of the above amendments and remarks, reconsideration and favorable action on all pending claims are respectfully requested. If any questions or issues remain, the Examiner is invited to contact the undersigned at the telephone number set forth below so that a prompt disposition of this application can be achieved.

If a fee is required for an extension of time which is not accounted for, such an extension is requested and the U.S.P.T.O. is authorized to withdraw from our Deposit Account Number 19-0741 any fee required.

Respectfully submitted,

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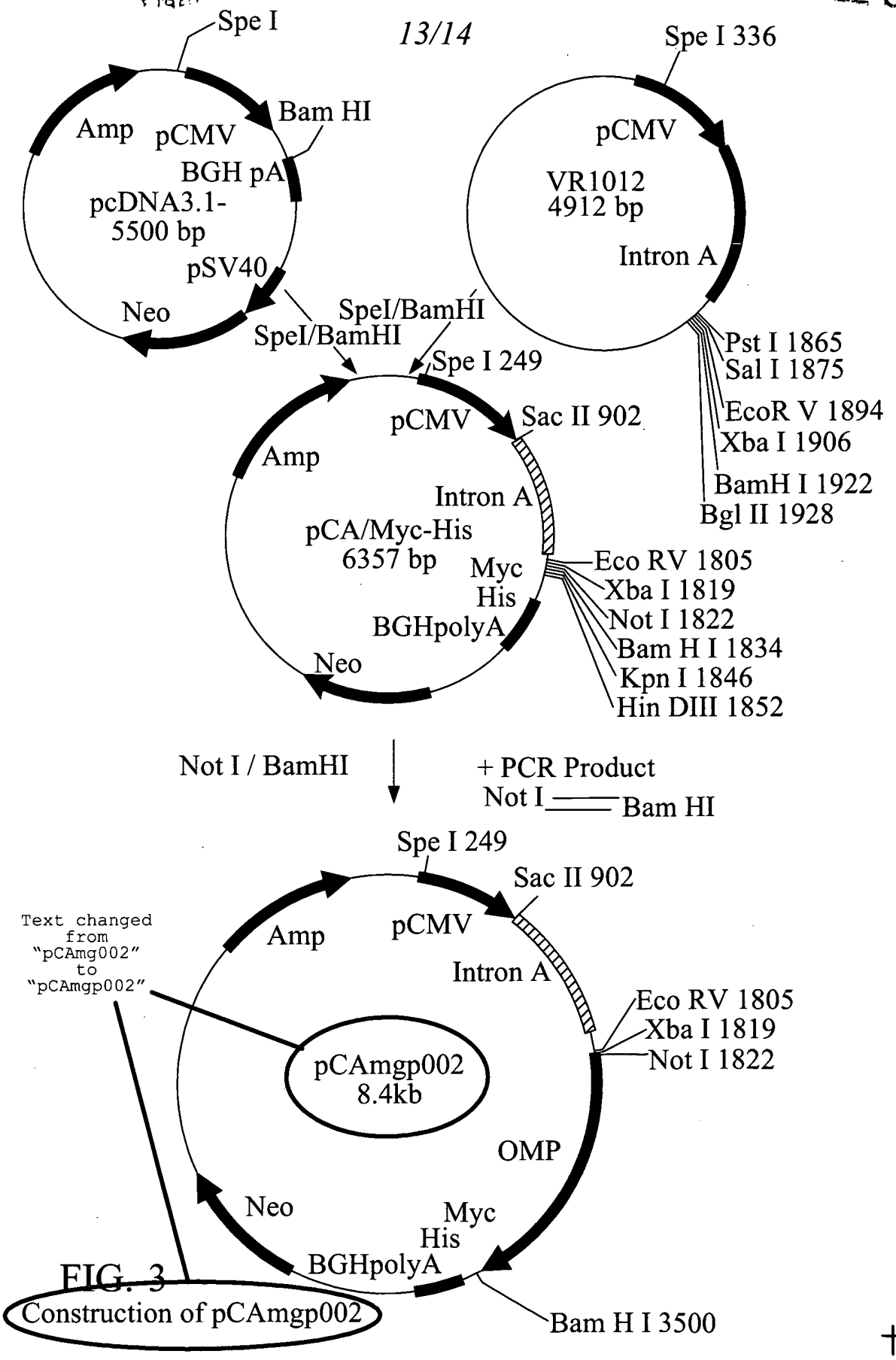

FIG. 3
Construction of pCAmgp002